

Application No. 10/796,522  
Amendment dated December 15, 2006  
Reply to Office Action of August 15, 2006

Docket No.: 01017/30016A

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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the applications:

Listing of Claims:

1.30. (canceled)

31. (Currently amended) A therapeutic composition comprising an amyloid-beta (A $\beta$ ) polypeptide [[and]] linked to a non-A $\beta$  polypeptide, and a sterile pharmaceutically acceptable carrier or excipient that is a diagnostic or therapeutic agent for a disorder of the central nervous system (CNS), wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are linked, wherein said composition is for treatment of a human patient that has been diagnosed with a CNS disorder.

32. (Canceled)

33. (Previously presented) The composition of claim 31, wherein said non-A $\beta$  polypeptide is an antibody.

34. (Previously presented) The composition of claim 33, wherein the antibody is a monoclonal antibody.

35. (Previously presented) The composition of claim 34, wherein the monoclonal antibody has specific binding affinity for amyloid comprising residues 1-39 of SEQ ID NO: 1.

36. (Previously presented) The composition of claim 33, wherein the antibody is a chimeric antibody.

37. (Previously presented) The composition of claim 33, wherein the antibody is a humanized antibody.

38. (Previously presented) The composition of claim 33, wherein said antibody is an Fab fragment.

39. (Previously presented) The composition of claim 33, wherein said antibody is a single chain Fv antibody fragment.

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40. (Previously presented) The composition of claim 33, wherein said antibody is an F(ab)<sub>2</sub> fragment.

41. (Previously presented) The composition of any one of claims 33, 34, 35 or 37, wherein the antibody is polyamine modified.

42. (Previously presented) The composition of claim 31, 34, 35 or 37 wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are covalently linked.

43. (Currently amended) The composition of claim 31, 34, 35 or 37, ~~69, 70 or 72~~ wherein said A $\beta$  polypeptide comprises residues 1-39 of SEQ ID NO: 1.

44. (Previously presented) The composition of claim 35 wherein said A $\beta$  polypeptide comprises residues 1-42 of SEQ ID NO: 1.

45. (Currently amended) The composition of claim 31, ~~34, 35 or 37~~ wherein said A $\beta$  polypeptide comprises residues 1-39 of SEQ ID NO: 1 in which one or more substitutions at position 5, 10, 13, 19 or 20 have been made.

46. (Previously presented) The composition of claim 45 wherein said substitution is selected from the group consisting of substituting the amino acid at position 5 of SEQ ID NO: 1 with Gly, substituting the amino acid at position 10 of SEQ ID NO: 1 with Tyr, substituting the amino acid at position 13 of SEQ ID NO: 1 with Arg, substituting the amino acid at position 19 of SEQ ID NO: 1 with Ile, Leu, Thr, Ser, Ala, Val, or Gly, and substituting the amino acid at position 20 of SEQ ID NO: 1 with Ile, Leu, Thr, Ser, Ala, Val, or Gly.

47. (Withdrawn) A composition comprising an A $\beta$  polypeptide, a humanized antibody having specific binding affinity for amyloid comprising residues 1-39 of SEQ ID NO: 1 and a pharmaceutically accepted carrier or excipient, wherein said A $\beta$  polypeptide comprises residues 1-39 of SEQ ID NO: 1.

48. (Currently amended) The composition of ~~any one of claims~~ claim 31, 34, 35, 37 or 47 which exhibits a permeability coefficient x surface area (PS) product of 2.3 x 10<sup>-6</sup> ml/g/sec or greater, wherein the PS product is determined after correction for the residual plasma volume (V<sub>p</sub>) occupied by the protein in blood vessels in different brain regions following an intravenous bolus injection.

49.-50. (Canceled)

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51. (Withdrawn and Currently amended) The composition of claim 31, 67, 70 or 72, wherein said non- $\text{A}\beta$  polypeptide is an enzyme.

52. (Withdrawn) The composition of claim 51, wherein said enzyme is an antioxidant enzyme.

53. (Withdrawn) The composition of claim 52, wherein said antioxidant enzyme is catalase or superoxide dismutase.

54. (Withdrawn and Currently Amended) The composition of claim 31, 67, 70 or 72, wherein said non- $\text{A}\beta$  polypeptide is leptin.

55. (Withdrawn and Currently Amended) The composition of claim 31, 67, 70 or 72, wherein said non- $\text{A}\beta$  polypeptide is a cytokine.

56. (Withdrawn) The composition of claim 55, wherein said cytokine is an interferon or an interleukin or a neurotrophic factor.

57. (Withdrawn and Currently Amended) A method of delivering the composition of claim 35, 47, 52 or 55, 67, 69, 70 or 72, to the brain of a patient having Alzheimer's disease, said method comprising administering to said patient an amount of said composition sufficient to cross the blood brain barrier of said patient.

58. (Withdrawn) A method of delivering the composition of claim 43 to the brain of a patient having Alzheimer's disease, said method comprising administering to said patient an amount of said composition sufficient to cross the blood brain barrier of said patient.

59. (Withdrawn/Currently amended) A method of diagnosing Alzheimer's disease in a patient, said method comprising a) administering a composition of claim [[35]] 69, 70 or 72 to said patient, wherein said composition is labeled, and b) detecting the presence or absence of said antibody bound to amyloid in the brain of said patient, wherein said patient is diagnosed with Alzheimer's disease based on the presence of labeled amyloid in the brain of said patient.

60. (Withdrawn) The method of claim 59, wherein said detecting step comprises diagnostic imaging.

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61. (Withdrawn) The method of claim 60, wherein said diagnostic imaging comprises positron emission tomography, gamma-scintigraphy, single photon emission computerized tomography, magnetic resonance imaging, functional magnetic resonance imaging, or magnetoencephalography.

62. (Withdrawn) The method of claim 60, wherein said diagnostic imaging comprises magnetic resonance imaging.

63. (Withdrawn) The method of claim 59, wherein said amyloid comprises  $\beta$ -amyloid plaques.

64. (Withdrawn) The method of claim 59, wherein said antibody is labeled with a contrast agent.

65. (Withdrawn) The method of claim 64, wherein said contrast agent is selected from the group consisting of gadolinium, dysprosium, and iron.

66. (Withdrawn) The method of claim 64, wherein the contrast agent is gadolinium.

67. (Previously presented) A composition comprising an amyloid-beta (A $\beta$ ) polypeptide and a non-A $\beta$  polypeptide, wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are covalently linked.

68. (Previously presented) The composition of claim 67, wherein said non-A $\beta$  polypeptide is an antibody.

69. (New) A composition comprising an human amyloid-beta (A $\beta$ ) polypeptide and a non-A $\beta$  polypeptide, wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are linked;

wherein said non-A $\beta$  polypeptide is a monoclonal antibody having specific binding affinity for amyloid comprising residues 1-39 of SEQ ID NO: 1; and,

wherein said non-A $\beta$  polypeptide is a diagnostic or therapeutic agent for a disorder of the central nervous system (CNS).

70. (New) A composition comprising an human amyloid-beta (A $\beta$ ) polypeptide and a non-A $\beta$  polypeptide, wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are linked, wherein

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said A $\beta$  polypeptide comprises residues 1-39 of SEQ ID NO: 1 in which one or more substitutions at position 5, 10, 13, 19 or 20 have been made.

71. (New) The composition of claim 70, wherein said substitution is selected from the group consisting of substituting the amino acid at position 5 of SEQ ID NO: 1 with Gly, substituting the amino acid at position 10 of SEQ ID NO: 1 with Tyr, substituting the amino acid at position 13 of SEQ ID NO: 1 with Arg, substituting the amino acid at position 19 of SEQ ID NO: 1 with Ile, Leu, Thr, Ser, Ala, Val, or Gly, and substituting the amino acid at position 20 of SEQ ID NO: 1 with Ile, Leu, Thr, Ser, Ala, Val, or Gly.

72. (New) A composition comprising an human amyloid-beta (A $\beta$ ) polypeptide and a non-A $\beta$  polypeptide, wherein said A $\beta$  polypeptide and said non-A $\beta$  polypeptide are linked, which exhibits a permeability coefficient  $\times$  surface area (PS) product of  $2.3 \times 10^{-6}$  ml/g/sec or greater, wherein the PS product is determined after correction for the residual plasma volume (Vp) occupied by the protein in blood vessels in different brain regions following an intravenous bolus injection.